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Depression, anxiety, and body image after treatment for invasive stage one epithelial ovarian cancer

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ABSTRACT

Background:

Diagnosis of epithelial ovarian cancer (EOC) in young women has major implications including those to their reproductive potential. We evaluated depression, anxiety and body image in patients with stage I EOC treated with fertility sparing surgery (FSS) or radical surgery (RS). We also investigated fertility outcomes after FSS.

Methods:

A retrospective study was undertaken in which 62 patients completed questionnaires related to anxiety, depression, body image and fertility outcomes. Additional information on adjuvant therapy after FSS and RS and demographic details were abstracted from medical records. Both bi and multivariate regression models were used to assess the relationship between demographic, clinical and pathological results and scores for anxiety, depression and body image.

Results:

Thirty-nine patients underwent RS and the rest, FSS. The percentage of patients reporting elevated anxiety and depression (subscores $\geq$ 11) were 27 % and 5% respectively. The median (inter quartile range) score for body image scale (BIS) was 6 (3-15). None of the demographic or clinical factors examined showed significant association with anxiety and BIS with the exception of 'time since diagnosis'. For depression, post-menopausal status was the only independent predictor. Among those 23 patients treated by FSS, 14 patients tried to conceive (7 successful), resulting in 7 live births, one termination of pregnancy and one miscarriage.

Conclusion:

This study shows that psychological issues are common in women treated for stage I EOC. Reproduction after FSS is feasible and lead to the birth of healthy babies in about half of patients who wished to have another child. Further prospective studies with standardised instruments are required.

INTRODUCTION

Approximately 23% of all stage I epithelial ovarian cancers (EOCs) occur in women who are younger than 40 years of age [1]. The standard treatment for apparent stage I EOC consists of a total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO) and surgical staging plus adjuvant chemotherapy if indicated. However, radical treatment has major implications for patients' childbearing potential. As an alternative for those patients who wish to preserve fertility, conservative surgery (fertility sparing surgery (FSS)) has been described previously demonstrating encouraging survival results [2-5].

For patients, quality of life (QOL) is considered the second most important outcome of cancer treatment and patients should be informed about the likely impact on QOL when different treatment options are considered [6]. Across all stages of disease, nearly 30% of gynaecological cancer patients report psychological distress, and symptoms of depression, anxiety and hostility [7]. More recently, detriments to women's body image through invasive surgery have been reported [8], as cancer and subsequent treatment have negative impact on self-esteem and perception of the body [9-11]. Although the description of 'body image' is not defined universally, the term encompasses body integrity, outer appearance, proper body functioning, and the ability to relate to others [12-15].

To date, no studies investigated anxiety, depression, and body image among young women treated for stage I epithelial ovarian cancer (EOC) and demographic and clinical factors associated with better well-being. The purpose of this study therefore was to

evaluate factors associated with anxiety, depression and body image among young patients with stage I EOC who were treated by either FSS or RS. We also report on the reproductive outcomes of those patients treated by FSS.

MATERIALS AND METHODS

Subjects

All patients with stage IA, IB and IC histologically confirmed invasive EOC, between 18 and 45 years at time of diagnosis, who were treated at the Queensland Centre for Gynaecological Cancer (QCGC), Australia, from 01 April 1982 until 01 June 2004 were screened for eligibility to participate. Exclusion criteria included: (1) age at diagnosis > 45 years; (2) deceased at time of the survey or lost to follow-up; (3) diagnosis of other ovarian tumour types (borderline or germ cell tumours); (4) prior hysterectomy; (5) previous or other concomitant malignancy; and (6) incomplete chart information regarding diagnosis, stage or surgical treatment. Tumours were staged according to the staging system of the International Federation of Gynaecology and Obstetrics (FIGO). All eligible survivors were sent standardised questionnaires (detailed below) and those who responded were included into this study.

This study was approved by the local Human Research Ethics Committee (approval number 2005/013) of the Royal Brisbane and Women's Hospital.

Surgical and adjuvant treatment

RS included total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO), omentectomy and pelvic/para-aortic lymphadenectomy. Peritoneal washings,

diaphragmatic cytology and thorough exploration of the peritoneal cavity, including peritoneal biopsies were performed as part of the surgical staging procedure. FSS consisted of a unilateral salpingo-oophorectomy (SO), infracolic omentectomy, appendectomy, endometrial curettage, multiple peritoneal biopsies, peritoneal cytology, and pelvic and para-aortic lymphadenectomy. FSS was not performed in patients with bilateral EOC.

Adjuvant chemotherapy was offered to all patients with incomplete surgical staging, bilateral ovarian involvement, clear-cell histological type, and higher grade tumours. The remainder of patients were offered adjuvant chemotherapy on an ad-hoc basis, at the discretion of the treating consultant. Surgical, pathological and chemotherapeutic details were abstracted from hospital medical records.

Measures

A standardised questionnaire package queried the following: (1) demographics; (2) reproductive function, fertility outcomes and offspring; (3) relationship status; and (4) the patient's recall of her psychological functioning, in particular related to symptoms of anxiety and depression, prior to and after the diagnosis of ovarian cancer. Specifically, patients were asked whether they had ever or were taking medication to treat or prevent anxiety and or treat depression (yes/no), whether they thought to have suffered from anxiety/depression symptoms before or after their diagnosis and treatment for cancer (before/after/both/never) and whether they had sought counselling or therapy for anxiety or depression (before/after/both/never) and/or whether they were currently receiving counselling or therapy for anxiety or depression (yes/no).

The Hospital Anxiety and Depression Scale (HADS) was used to assess the patients' current (during the past week) level of psychological functioning. The HADS, developed by Zigmond and Snaith [16] in 1983, is an assessment scale to detect states of anxiety and depression in patients attending a hospital medical outpatient clinic, while it excludes potential somatic symptoms often associated with anxiety and depression but also common as a result of cancer treatment, such as fatigue. The HADS is subdivided into an anxiety subscale (HADS-A) and a depression subscale (HADS-D). Both subscales contain seven items, scored on a four-point scale from 0 to 3, with higher scores indicating greater levels of distress. The designers of the HADS advised to use a cut-off score of $\geq$ 11 to identify patients who have a high probability of suffering from a mood disorder, i.e. being a likely 'case'[16].

In addition to HADS, the Body Image Scale (BIS) questionnaire was completed by each patient. The BIS is a ten-item assessment scale designed to be applicable to patients with cancer of any site and any form of cancer treatment. The items cover affective, behavioural and cognitive issues, rated by the patient over the last week on a four-point scale from "not at all" to "very much". The BIS score is the total ratings of each item, ranging from 0 to 30, with higher scores representing a worse body image. A cut-off score for body image disturbance is currently not available [8].

The questionnaires were sent to all patients at the same time (cross-sectional), with patients' time since diagnosis ranging from one to 23 years (median, 8.3 years). We also asked patients about their treatment outcomes after fertility sparing surgery.

Statistical analysis

Statistical analyses were performed using Stata, version 10.1 (Statacorp, College Station, Texas, USA). Bivariate and multiple linear regression analyses were used to investigate associations between HADS and BIS scores with socio-demographic, and oncological characteristics. Age at diagnosis, time since diagnosis, educational level, occupational category, post-menopausal status, types of surgery, FIGO stages, histological tumour type and grade were the variables evaluated in bivariate analyses. All the variables associated at a significance level less than 0.2 in the bivariate analysis were entered simultaneously into subsequent multivariate models. Analyses were separately done for HADS-A, HADS-D and BIS scores.

RESULTS

Patients

One-hundred-and-eight patients had had treatment for stage I EOC. Sixty four patients were eligible to participate in this study, and 62 (97%) patients completed the questionnaires. Forty-four patients met our exclusion criteria: 18 patients were lost to follow-up; 13 patients had incomplete information in their medical records; 9 patients had other ovarian tumour types; 4 patients had previous or concomitant malignancy.

Socio-demographic and oncological characteristics of the patients are shown in Table 1. Thirty-nine patients underwent RS whereas twenty-three patients had FSS. Nearly 48% of patients had had university education. Fifty percent of patients considered their occupation as ‘skilled’. Forty-five (73.8%) patients were in a relationship at the time of

diagnosis. At time of the survey, 37 patients were in the same relationship as they were at the time of diagnosis, and 11 patients had another or new relationship.

Anxiety and depression at the time of diagnosis

Thirty-nine (62.9%) patients reported to have suffered from depression and or anxiety symptoms at the time of their diagnosis/treatment (Table 2). Thirty five (90%) of these patients had sought therapy for their anxiety and or depression. Twenty three patients had had counselling for depression and or anxiety. Twenty seven patients reported that they took medications for depression and 25 patients were prescribed medication for anxiety. At the time of the survey, 12 patients were on medication for depression/anxiety.

Anxiety, Depression and Body Image at the time of the survey: The mean (SD) scores for HADS-A and HADS-D were 7.4(4.4) and 3.4(3.9) respectively. Overall, 27% of the patients had anxiety subscale score ≥ 11 (indicating elevated anxiety levels) and 5% of patients had depression subscale score ≥ 11 (indicating depression). The mean (SD) BIS score was 8.8 (7.6).

Bivariate association of different socio-demographic and oncological variables with HADS-A, HADS-D and BIS scores are shown in Table 2. Time since diagnosis showed significant ($p<0.02$) inverse association with all these three scores. University education and certain histological tumour types also exhibited significant association with BIS scores. On multi-variate analyses, for HADS-A time since diagnosis was the only independent factor that remained significant decreasing reported anxiety scores by 0.21

points (95% CI 0.02 - 0.40; p = 0.02) for each year since diagnosis after adjusting for university education and histological type. For HADS-D, post-menopausal status increased the risk of depression by 3.4 points (95% CI = 0.54-6.21; p=0.02) after adjusting for time since diagnosis, histological type and grade. For BIS, time since diagnosis was the only independent predictor after adjusting for time since diagnosis, university education, skilled occupational status, histological type and grade, with women's body image improving by 0.49 BIS points for each year since diagnosis (95% CI 0.15-0.83) p=0.005).

Pregnancies after FSS

Changes in menstrual pattern following initial therapy occurred in 11 (47.8%) of the FSS-patients: three patients were amenorrhoeic for less than six months; two patients for more than six months; and six patients experienced other changes in their menstrual pattern.

Of the 23 patients who had FSS, 14 (60.9%) patients tried to conceive, for a median period of 12 months (range 2-312 months). Four (28.6%) patients used fertility drugs while trying to conceive: three with an assisted reproductive technology and one to assist ovulation. Finally, eight pregnancies were achieved by seven patients with seven healthy children (Table 3). Three of these patients had chemotherapy before they became pregnant; despite this, none of the babies had any congenital anomalies.

Additional treatment

Overall, sixteen patients (25.8%) required additional surgery after their initial therapeutic surgery, including RS after initial FSS, diagnostic procedures to screen for

recurrence and management of complications. A higher percentage of patients treated by FSS (n=9, 39.1%) required additional surgeries consisting of hysterectomy and or salpingo-oophorectomy. Of the nine FSS patients requiring additional surgery, three had become pregnant prior to their pelvic clearance.

Twenty-six patients (41.9%) had chemotherapy as part of their treatment. Of these patients treated by chemotherapy, 18 (69.2%) patients reported long-term adverse effects. Adverse effects reported were paresthesia in hands and/or feet (n=9), muscular and/or joint pains (n=9), and other adverse effects (n=7). None of the patients developed renal failure. One patient required adjuvant pelvic radiotherapy and vaginal vault brachytherapy.

DISCUSSION

Young women diagnosed with EOC face several concerns that may impact on their mental health and quality of life, including threats to their reproductive potential. Indeed, the current study shows that more than 60% of women treated for stage I EOC recall being depressed and/or anxious at the time of their initial diagnosis and treatment, and 27% and 5%, respectively, still reported elevated anxiety or depression scores, up to 23 years after surgery.

Although the literature on QOL in patients with EOC is expanding, the evidence about psychosocial well-being after different surgical and adjuvant treatments is still sparse particularly for young women. Among the few studies reported to date, a variety of assessment instruments have been used to investigate these issues, and the studies did

not differentiate between patients diagnosed at early or late stages of EOC, making comparison of the literature complicated (Table 4). In addition, none of the previous studies investigated whether receiving FSS or RS influenced QOL outcomes among patients treated for early EOC.

Our results indicate that 'time since diagnosis' is inversely related to anxiety and depression, and this result is consistent with those presented by Norton et al indicating that women's mental well-being improves as they recover from a diagnosis of ovarian cancer [11]. Nevertheless, compared to the results from other studies which included patients with higher stage disease (Table 4), the percentage of stage I patients in our study with anxiety and depression at the time of diagnosis were relatively high. Possible explanations for this include population differences, recall bias, measurement and cultural differences. With regards to population, younger patients have been reported to perceive cancer as an "out of order" experience compared to older patients and thus experience larger detriments to their QOL [17]. The higher incidence of anxiety compared to depression after treatment for EOC is in accordance with the literature [11, 18-20].

Our results indicate that the type of surgery patients received (RS or FSS), did not significantly influence quality of life outcomes including body image. This differs from Stead et al [9] who showed that BIS differed between patients who had different types of hysterectomy and Liavaag et al [20] who reported higher body image disturbance on average (mean BIS score =15.3, SD 6.0) among 189 EOC patients compared to our study. The long time since treatment was received on average by the patients in this

study and the early stage disease may have contributed to this finding [8, 12]. The only other study investigating body image in patients treated for EOC used a different outcome measure and reported that the patients had positive feelings about their face and hair, and neutral feelings about their body appearance, abdomen, sexual organs and weight [21].

Reproductive outcomes

In the current study almost two-thirds (14 of 23 patients) who underwent FSS tried to conceive. The actual pregnancy rate of 34.8% (8/23) is comparable with other studies investigating fertility outcomes after FSS, with most studies reporting pregnancy rates between 30 and 40% [2-5]. We observed a trend for FSS-patients to require more additional surgeries compared to RS treated patients. Demand from patients for RS after completing their family planning could explain most of this difference. Only one of the FSS-patients required additional surgery to investigate recurrence.

Strengths and limitations

This is the first study of depression, anxiety and body image scores in young patients with stage 1 EOC treated by FSS or RS. These results have to be interpreted with caution due to the retrospective nature of our study, the small sample size and non-random allocation of patients to FSS and RS. Eighteen patients were lost to follow up/dead at the time of the survey, and these patients may have had worse outcomes than those who were contactable. Patients were treated up to 23 years prior to receiving our questionnaire, which is another limitation of this study (recall bias). In addition, treatment modalities might have improved including the introduction of platinum based

therapy, which make it possible that more recently treated patients have diverse treatment outcomes. Only one of the patients underwent laparoscopic procedure and advantages of laparoscopic versus open procedure could not be investigated.

Conclusion

Our study shows that symptoms of anxiety and depression are common in women treated for stage I epithelial ovarian cancer especially at the time of diagnosis and initial treatment. However, even after several years of treatment for stage I EOC, almost 27% of women report elevated levels of anxiety. Reproduction after FSS is feasible and leads to the birth of a healthy baby in more than 30% of patients. A prospective study which measures the trajectory of depression and anxiety depending on whether RS or FSS for early stage ovarian cancer is received could be important to further establish protective factors for psychological distress.

Declaration of interest

All the authors declare that there are no conflicts of interest.

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Tables

TABLE 1. CHARACTERISTICS OF PATIENTS IN THIS STUDY

Characteristics	n (%)
Age at diagnosis, years, mean (SD)	36.5 (7.5)
Time since diagnosis, years, mean (SD)	10.0 (5.6)
Gravidity, mean (SD)	2.6 (1.8)
Post-menopausal	9 (15.5)
Surgery	
Fertility sparing surgery (FSS)	23 (37.1)
Radical Surgery	39 (62.9)
Highest education level	
Less than secondary school	17 (27.9)
Secondary school	14 (22.9)
< 3 years of study[a]	16 (26.2)
3-4 years of study[b]	10 (16.4)
>4 years of study[c]	4 (6.6)
Occupation	
Professional[d]	23 (37.1)
Clerical[e]	8 (12.9)
Semi-skilled[f]	9 (14.5)
Home work[g]	15 (24.2)
Other	4 (6.5)
FIGO stage	
IA	38 (61.3)
IB	2 (3.2)
IC	22 (35.5)
Histology	
Mucinous	30 (48.4)
Serous	9 (14.5)
Endometrioid	17 (27.4)
Other	6 (9.7)
Differentiation	
Well	25 (40.3)
Moderately	15 (24.2)
Poorly	6 (9.7)
Unknown	16 (25.8)

a. Completed trade certificate or qualification requiring less than 3 years of study.
b. Academic or professional qualification requiring 3 or 4 years of university study.
c. Academic or professional qualification requiring more than 4 years of university study.
d. Professional or managerial.
e. Clerical or sales.
f. Semi-skilled includes semi-skilled and unskilled patients.
g. Home work includes retired patients and patients with home duties.

TABLE 2. BIVARIATE ASSOCIATION OF ANXIETY, DEPRESSION AND BODY IMAGE SCORES WITH PARTICIPANT CHARACTERISTICS

	Anxiety				Depression				Body Image Scale			
Characteristics	Coeff	95% CI		p	Coeff	95% CI		p	Coeff	95% CI		p
Age at diagnosis, years	-0.04	-0.19	0.11	0.608	0.06	-0.07	0.20	0.339	-0.02	-0.28	0.24	0.872
Time since diagnosis, years	-0.24	-0.43	-0.05	0.014	-0.22	-0.39	-0.05	0.011	-0.56	-0.88	-0.24	0.001
Fertility sparing surgery Vs radical surgery	0.56	-1.76	2.88	0.631	-0.37	-2.45	1.70	0.721	0.89	-3.17	4.94	0.663
Attended university	1.83	-0.36	4.03	0.100	0.16	-1.85	2.17	0.875	5.57	1.92	9.22	0.003
Skilled occupation	-0.13	-2.37	2.12	0.909	-0.97	-2.96	1.02	0.335	3.19	-0.64	7.03	0.101
Post-menopausal	0.13	-3.12	3.37	0.938	2.41	-0.43	5.25	0.094	3.14	-2.46	8.73	0.266
FIGO 1B and 1C (1A as reference)	-0.42	-1.56	0.73	0.469	-0.27	-1.29	0.76	0.606	0.27	-1.74	2.28	0.787
Histology (Mucinous as reference)												
Endometrioid Vs Mucinous	-1.89	-4.48	0.70	0.149	-0.36	-2.74	2.01	0.76	-2.01	-6.42	2.41	0.367
Serous Vs Mucinous	2.06	-1.18	5.29	0.209	1.29	-1.68	4.26	0.389	4.70	-0.82	10.22	0.094
Others Vs Mucinous	-2.33	-6.14	1.48	0.225	-2.43	-5.93	1.07	0.169	-6.63	-13.13	-0.13	0.046
Differentiation (Well differentiated as reference)												
Moderately differentiated Vs Well diff	1.29	-1.54	4.13	0.365	-0.72	-3.28	1.84	0.575	-1.63	-6.63	3.37	0.518
Poorly differentiated Vs Well diff	-1.31	-5.26	2.64	0.511	-1.32	-4.88	2.24	0.461	0.51	-6.46	7.47	0.885
Unknown differentiation Vs Well diff	-1.70	-4.48	1.08	0.226	-2.20	-4.70	0.31	0.085	-3.97	-8.88	0.93	0.110

FIGO: International Federation of Gynaecology and Obstetrics

TABLE 3. CHARACTERISTICS OF THE CONCEPTIONS AFTER FSS

(7 OF 14 PATIENTS WHO TRIED TO CONCEIVE)

Pt	Conception (n=8)	Outcome	Term (weeks)	Fertility treatment	Chemotherapy	Congenital anomalies
1	1	Single baby	40	No	Yes	No
2	1	Single baby	40	No	Yes	No
3	1	TOP	10	No	No	No
4	1	Single baby	40	No	No	No
	2	Single baby	40	No	No	No
5	1	Single baby	40	No	No	No
6	1	Miscarriage	12	Yes	No	No
7	1	Twins	28	No	Yes	No

FSS = fertility sparing surgery; Pt = patient; TOP = termination of pregnancy.

TABLE 4. REVIEW OF THE LITERATURE FOR DEPRESSION AND ANXIETY IN OVARIAN CANCER

Author	Population	N	Stage I (%)	Used Measures		Results
				Depression	Anxiety	
Kornblith [19] 1995	Ovarian cancer patients (74% hospitalized)	151	14[a]	MSAS, MHI-38	MSAS, MHI-38	MSAS: > $^1/_3$ of patients had moderate to severe symptoms of anxiety and depression MHI: 17% highly depressed, 22% highly anxious
Bodurka [22] 2000	EOC patients (94.3% outpatient)	246	26[a]	CES-D	STAI	21% met the cut-off criteria for clinical evaluation of depression 29% scored above the 75th percentile for anxiety
Wenzel [23] 2002	> 5 years stage I and II ovarian cancer survivors	49	77.6	CES-D		6% met cut-off criteria for significant depressive symptoms
Hipkins [18] 2004	EOC patients at the end of chemotherapy and with 3 months follow-up	63	22	HADS	HADS	Significant increase in anxiety scores ≥ 8 (38% to 47%) and reduction in depression scores ≥ 8 (33% to 19%) over follow-up time
Norton [11] 2004	Ovarian cancer patients	143	14	BDI, MHI-18	MHI-18	BDI: 20% had moderate to severe depressive symptoms MHI: 23% had moderate to high distress, with significantly higher mean levels of anxiety than depressive symptoms
Parker [24] 2006	EOC patients starting chemotherapy	126	8	CES-D	STAI	25% met cut-off criteria for significant depressive symptoms Mean anxiety score was at the 69th percentile compared with normative samples
De Moor [25] 2006	EOC patients starting chemotherapy	90	8	CES-D	STAI	Mean depression score 11.0 (SD 4.95)[b], mean anxiety score 36.11 (SD 8.61)[b], (no cut-off scores mentioned)
Liavaag [20] 2007	EOC patients with > 18 months survival versus controls	189	43	HADS	HADS	Mean depression score 3.1, mean anxiety score 5.6 Anxiety levels were significantly higher and depression levels lower than in controls

N = number of patients included in the study; EOC = epithelial ovarian cancer; SD = standard deviation.
MSAS = Memorial Symptom Assessment Scale; MHI = Mental Health Inventory; CES-D = Centre for Epidemiologic Studies-Depression scale; STAI = Spielberger State and Trait Anxiety Inventory for Adults; HADS = Hospital Anxiety and Depression Scale; BDI = Beck Depression Inventory.
a. Includes stage I and II. b. Results presented for stage I and II together. Stage I and II make up 15% of the total number of patients.